

4-14-06

1fw



Docket No.
000605/0002
(MWS:BPL)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Schubert et al.

Group Art Unit: 1648

Application No.: 10/510,355

Examiner: Franco Salvoza

Filed: April 28, 2005

For: AGENTS FOR TREATING FLAVIVIRIDAE INFECTIONS

Date: April 16, 2006

**CERTIFICATE OF MAILING
BY "EXPRESS MAIL" (37 C.F.R. § 1.10)**

Mail Stop Amendment

Commissioner for Patents

PO Box 1450

Alexandria, Virginia 22313-1450

Sir:

I hereby certify that the following correspondence:

Information Disclosure Statement (7 pgs) and PTO FORM 1449 (4 pgs)

is being deposited on April 13, 2006 with the United States Postal Service for "Express Mail Post Office to Addressee" delivery under 37 C.F.R. § 1.10 in an envelope bearing sufficient postage and addressed to:

**Mail Stop
Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450.**

Benjamin Liu

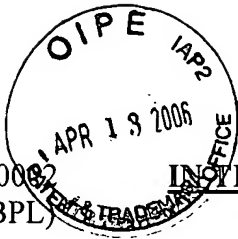
(Typed Or Printed Name Of Person Mailing Correspondence)

(Signature Of Person Mailing Correspondence)

EV 082949240 US

("Express Mail" Mailing Label Number)

000605.0002
(MWS:BPL)



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : **Schubert et al.**

Application No.: **10/510,355**

Art Unit No. : **1648**

Filed : **April 28, 2005**

Examiner : **Franco Salvoza**

For : **AGENTS FOR TREATING FLAVIVIRIDAE INFECTIONS**

Date: April 13, 2006

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

In compliance with the duty of disclosure under 37 C.F.R. § 1.56 and in accordance with the practice under 37 C.F.R. §§ 1.97 and 1.98, the Examiner's attention is directed to the documents listed on the enclosed Information Disclosure Statement by Applicant (Form PTO-1449). Consistent with current practice, and in accordance with 37 C.F.R. § 1.98(a)(2)(ii) as revised at 69 Fed. Reg. 56481 (September 21, 2004), copies of the cited U.S. patents have not been submitted. 02/30455

Copies of the following documents are enclosed for your convenience:

WO 99/22729

DE 10149398 -Abstract

WO 96/13266

WO 02/30455

Adams, J; Behnke, M; Chen, S; Cruickshank, AA; Dick, RL; Grenier, L; Klunder, JM; Ma, Y. T; Plamondon, L; Stein, RL (1998). Potent and selective inhibition of the proteasome: dipeptidyl boronic acids. *Bioorg. Med. Chem. Lett.* **8**:333-338.

Adams, J; Palombella, VJ; Sausville, EA; Johnson, J; Destree, A; Lazarus, DD; Maas, J; Pien, CS; Prakash, S; Elliott, PJ (1999). Proteasome inhibitors: a novel class of potent and effective antitumor agents. *Cancer Res.* **59**:2615-2622.

Adams, J; Palombella, VJ; Elliot, PJ (2000). Proteasome inhibition: a new strategy in cancer treatment. *Investigational New Drugs* **18**:109-121.

Adams, J; Stein, R (1996). Novel inhibitors of the proteasome and their therapeutic use in inflammation. *Annu. Rep. Med. Chem.* **31**:279-288.

Agnello, V, Abel, G, Elfahal, M, Knight, GB, Zhang, QX; (1999). Hepatitis C virus and other flaviviridae viruses enter cells via low density lipoprotein receptor. *Proc Natl Acad Sci USA.* **96**:12766-71.

Agnello, V; (2000). Mixed cryoglobulinemia and other extrahepatic manifestations of hepatitis C virus infections. In: Liang, TJ, Hoonagle JH, eds. *Hepatitis C*. San Diego: Academic Press: 295-314.

Baldwin, AS (1996). The NF-kappa B and I kappa B proteins: new discoveries and insights. *Annu. Rev. Immunol.* **14**:649-683.

Barton, DJ, Flanagan JB; (1993). Coupled translation and replication of poliovirus RNA *in vitro*: synthesis of functional 3D polymerase and infectious virus. *J. Virol.* **67**: 822-831.

Behrens, SE, Grassmann, CW, Thiel, HJ, Meyers, G, Tautz, N; (1998). Characterization of an autonomous subgenomic RNA-replicon of a pestivirus. *J. Virol.* **72**: 2364-2372.

Bukh, J, Miller RH, Purcell, RH; (1995). Genetic heterogeneity of hepatitis C virus: quasispecies and genotypes. *Sem. Liver Dis.* **15**: 41-63.

Burke, DS, Monath, TP; (2001). Flaviviruses. In: *Virology*, fourth edition edited by B.N. Fields, Lippincott-Raven Philadelphia, New York: 1043-1125.

Ciechanover, A (1998). The ubiquitin-proteasome pathway: on protein death and cell live. *EMBO J.* **17**:7151-7160.

Ciechanover, A, Orian, A, Schwartz, AL; (2000). The ubiquitin-mediated proteolytic pathway: mode of action and clinical implications. *J. Cell Biochem. Suppl.* **34**: 40-51.

Coux, O; Tanaka, K; Goldberg, AL (1996). Structure and functions of the 20S and 26S

proteasomes. *Annu. Rev. Biochem.* **65**: 801-847.

Dubuisson, J, Hsu, HH, Cheung, RC, Greenberg, HB, Russell, DG, Rice, CM; (1994). Formation and intracellular localization of hepatitis C virus envelope glycoprotein complexes expressed by recombinant vaccinia and Sindbis virus. *J. Virol.* **68**: 6147-6160.

Elliott, PJ, Ross JS; (2001). The proteasome: a new target for novel drug therapies. *Am J Clin Pathol.* **116**:637-46.

Elliott, PJ; Pien, CS; McCormack, TA; Capman, ID; Adams, J (1999). Proteasome inhibition: a novel mechanism to combat asthma. *J. Allergy Clin. Immunol.* **104**: 294-300.

Fenteany, G; Standaert, RF; Lane, WS; Choi, S; Corey, EJ; Schreiber, SL (1995). Inhibition of proteasome activities and subunit-specific amino-terminal threonine modification by lactacystin. *Science* **268**: 726-731.

Frankel, A; Man, S; Elliott, P; Adams, J; Kerbel, RS (2000). Lack of multicellular drug resistance observed in human ovarian and prostate carcinoma treated with the proteasome inhibitor PS-341. *Clinical Cancer Res.* **6**:3719-3728.

Fuerst, TR, Niles, EG, Studier, FW, Moss B; (1986). Eukaryotic transient-expression system based on recombinant vaccinia virus that synthesizes bacteriophage T7 RNA polymerase. *Proc. Natl. Acad. Sci. USA* **83**: 8122-8126.

Grassmann, CW, Isken, O, Behrens SE; (1999). Assignment of the multifunctional NS3 protein of bovine viral diarrhea virus during RNA replication: an in vivo and in vitro study. *J. Virol.* **73**: 9196-9205.

Grassmann, CW, Isken, O, Tautz, N, Behrens SE; (2001). Genetic analysis of the pestivirus nonstructural coding region: defects in the NS5A unit can be complemented *in trans*. *J. Virol.* **75**: 7791-7802.

Hanada, M; Sugawara, K; Kaneta, K; Toda, S; Nishiyama, Y; Tomita, K; Yamamoto, H; Konishi, M; Oki, T (1992). Epoxomicin, a new antitumor agent of microbial origin. *J. Antibiot. (Tokyo)* **45**:1746-1752.

Harty, RN; Brown, ME; Wang, G; Huibregtse, J; Hayes, FP; (2000). A PPxY motif within the VP40 protein of Ebola virus interacts physically and functionally with a ubiquitin ligase: implications for filovirus budding. *Proc. Natl. Acad. Sci. USA* **97**: 13871-13876.

Hershko, A; Ciechanover, A; (1998). The ubiquitin system. *Annu. Rev. Biochem.* **67**: 425-479.

Higashitsuji, H; Itoh, K; Nagao, T; Dawson, S; Nonoguchi, K; Kido, T; Mayer, RJ; Arai, S; Fujita, J; (2000). Reduced stability of retinoblastoma protein by gankyrin, an oncogenic ankyrin-repeat protein overexpressed in hepatomas. *Nat Med.* 6:96-99.

Koeck J, Nassal M, MacNelly S, Baumert TF, Blum HE, von Weizsaecker F; (2001). Efficient infection of primary *Tupaia* hepatocytes with purified human and woolly monkey hepatitis B virus. *J. Virol.* 75:5084-5089.

Krueger, M; Beger, C; Welch, PJ; Barber, JR; Manns, MP; Wong-Staal, F; (2001). Involvement of Proteasome α -Subunit PSMA7 in Hepatitis C Virus Internal Ribosome Entry Site-Mediated Translation; *Mol. Cell. Biol.* Vol. 21 No. 24, p 8357-8364.

Lohmann, V, Koerner, F, Koch, JO, Herian, U, Theilmann, L., Bartenschlager R; (1999). Replication of subgenomic hepatitis C virus RNAs in a hepatoma cell line. *Science* 285:110-113.

Lightcap, ES; McCormack, TA; Pien, CS; Chau, V; Adams, J; Elliott, PJ (2000). Proteasome inhibition measurements: clinical application. *Clin. Chem.* 46:673-683.

Lindenbach, BD, Rice, CM; (2001). Flaviviridae: the viruses and their replication. In: *Virology*, fourth edition edited by B.N. Fields, Lippincott-Raven Philadelphia, New York: 991-1042.

Major, ME, Rehmann, B, Feinstone, SM; (2001). Hepatitis C viruses. In: *Virology*, fourth edition edited by B.N. Fields, Lippincott-Raven, Philadelphia, New York: 1127-1161.

Meng, L; Kwok, BH; Sin, N; Crews, CM (1999a). Eponemycin exerts its antitumor effect through the inhibition of proteasome function. *Cancer Res.* 59:2798-2801.

Meng, L; Mohan, R; Kwok, BH; Eloffson, M; Sin, N; Crews, CM (1999b). Epoxomicin, a potent and selective proteasome inhibitor, exhibits *in vivo* antiinflammatory activity. *Proc. Natl. Acad. Sci. USA.* 96 (18): 10403-10408.

Merola, M, Brazzoli, M, Cochiarella, F, Heile, JM, Helenius, A, Weiner, AJ, Houghton, M, Abrignani, S; (2001). Folding of Hepatitis C Virus E1 glycoprotein in a cell-free system. *J. Virol.* 75:11205-11217.

Meyers, G, Tautz, N, Becher, P, Thiel, H-J, Kuemmerer BM; (1996). Recovery of cytopathogenic and noncytopathogenic bovine viral diarrhea viruses from cDNA constructs. *J. Virol.* 70: 8606-8613.

Moormann, RJM, van Gennip, HGP, Miedema, GKL, Hulst, MM, van Rijn PA; (1996). Infectious RNA transcribed from an engineered full-length cDNA template of the genome

of a pestivirus. *J. Virol.* 70: 763-770.

Moradpour, D; Grabscheid, B; Kammer, AR; Schmidtke, G; Groettrup, M; Blum, HE; Cerny, A (2001). Expression of hepatitis C virus proteins does not interfere with major histocompatibility complex class I processing and presentation in vitro. *Hepatology* 33:1282-1287.

Palombella, VJ; Conner, EM; Fuseler, JW; Destree, A; Davis, JM; Laroux, FS; Wolf, RE; Huang, J; Brand, S; Elliott, PJ; Lazarus, D; McCormack, T; Parent, L; Stein, R; Adams, J; Grisham, MB; (1998). Role of the proteasome and NF-kappaB in streptococcal cell wall-induced polyarthritis. *Proc. Natl. Acad. Sci. USA* 95:15671-15676.

Palombella, VJ; Rando, OJ; Goldberg, AL; Maniatis, T; (1994). The ubiquitin-proteasome pathway is required for processing the NF-kappa B1 precursor protein and the activation of NF kappa B. *Cell* 78:773-785.

Pamer, E; Cresswell, P; (1998). Mechanisms of MHC class I-restricted antigen processing. *Annu. Rev. Immunol.* 16:323-358.

Patnaik, A, Chau, V, Wills, JW; (2000). Ubiquitin is part of the retrovirus budding machinery. *Proc. Natl. Acad. Sci. USA* 97:13069-13074.

Pietschmann, T, Lohmann, V, Kaul, A, Krieger, N, Rinck, G, Rutter, G, Strand, D, Bartenschlager, R; (2002) Persistent and transient replication of full-length hepatitis C virus genomes in cell culture. *J. Virol.* 76:4008-21.

Phillips, JB; Williams, AJ; Adams, J; Elliott, PJ; Tortella, FC (2000). Proteasome inhibitor PS-519 reduces infarction and attenuates leukocyte infiltration in a rat model of focal cerebral ischemia. *Stroke* 31:1686-1693.

Rehermann, B; Ferrari, C; Pasquinelli, C; Chisari, FV (1996). The hepatitis B virus persists for decades after patients' recovery from acute viral hepatitis despite active maintenance of a cytotoxic T-lymphocyte response. *Nat Med.* 2:1104-1108.

Rock, KL; Gramm, C; Rothstein, L; Clark, K; Stein, R; Dick, L; Hwang, D; Goldberg, AL (1994). Inhibitors of the proteasome block the degradation of most cell proteins and the generation of peptides presented on MHC class I molecules. *Cell* 78:761-771.

Rock, KL; Goldberg, AL (1999). Degradation of cell proteins and the generation of MHC class I-presented peptides. *Annu. Rev. Immunol.* 17:739-779.

Ruemenapf, T., Unger, G, Strauss, JH, and Thiel, HJ; (1993). Processing of the envelope glycoproteins of pestiviruses. *J. Virol.* 67: 3288-3294.

Schubert, U; Anton, LC; Gibbs, J; Norbury, CC; Yewdell, JW; Bennink, JR (2000b). Rapid degradation of a large fraction of newly synthesized proteins by proteasomes.

Nature **404**:770-774.

Schubert, U; Ott, DE; Chertova, EN; Welker, R; Tessmer, U; Princiotta, MF; Bennink, JR; Kraeusslich, H-G; Yewdell, JW (2000a). Proteasome inhibition interferes with gag polyprotein processing, release, and maturation of HIV-1 and HIV-2. *Proc. Natl. Acad. Sci. USA* **97**:13057-13062.

Schwartz, AL; Ciechanover, A (1999). The ubiquitin-proteasome pathway and pathogenesis of human diseases. *Annu. Rev. Med.* **50**:57-74.

Strack, B; Calistri, A; Accola, MA; Palu, G; Goettlinger, HG (2000). A role for ubiquitin ligase recruitment in retrovirus release. *Proc. Natl. Acad. Sci. USA* **97**:13063-13068.

Suzuki, R; Tamura, K; Li, J; Ishii, K; Matsuura, Y; Miyamura, T; Suzuki, T (2001). Ubiquitin mediated degradation of hepatitis C virus core protein is regulated by processing at its carboxyl terminus. *Virology* **280**:301-309.

Teicher, BA; Ara, G; Herbst, R; Palombella, VJ; Adams, J (1999). The proteasome inhibitor PS-341 in cancer therapy. *Clin. Cancer Res.* **5**:2638-2645.

Thiel, HJ, Plagemann, PGW, Moennig, V; (1996). Pestiviruses. In B.N. Fields, D.M. Knipe, and P.M. Howley (ed.), *Fields virology*. Raven Press, Philadelphia. Pa.: 1059-1074.

Trautwein, C; Manns, M (2001). Antivirale Therapie der chronischen Virushepatitis. *Internist* **42**:913-923.

Yagi, T; Hardin, JA; Valenzuela, YM; Miyoshi, H; Gores, GJ; Nyberg, SL (2001). Caspase inhibition reduces apoptotic death of cryopreserved porcine hepatocytes. *Hepatology* **33**:1432-40.

Yu, H, Grassmann, CW, Behrens SE; (1999). Sequence and structural elements at the 3' terminus of bovine viral diarrhea virus genomic RNA: functional role during RNA replication. *J. Virol.* **73**: 3638-3648.

Yu, H, Isken, O, Grassmann, CW, Behrens SE; (2000). A stem-loop motif formed by the immediate 5'-terminus of the bovine viral diarrhea virus genome modulates translation as well as replication of the viral RNA. *J. Virol.* **74**: 5825-5835.

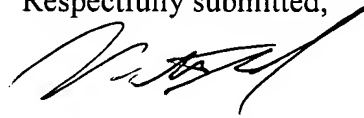
Zhao, X, Tang Z, Klumpp B, Wolff-Vorbeck, G, Barth H, Levy S, von Weizsaecker, F, Blum HE, Baumert TF; (2002). Primary hepatocytes of *Tupaia belangeri* as a potential model for hepatitis C virus infection *J. Clin. Invest.* **109**: 221-232.

Filed on April 28, 2005

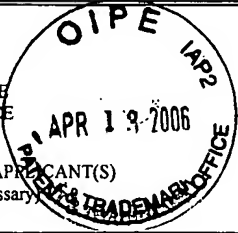
It is respectfully requested that the above information be considered by the Examiner and that a copy of the enclosed Information Disclosure Statement by Applicant (Form PTO-1449) be returned indicating that such information has been considered.

To date, Applicants have not received the first Office Action on the merits, so this Information Disclosure is believed to be filed under 37 C.F.R. § 1.97(b)(3). Therefore, no fee is deemed necessary in connection with the filing of this Supplemental Information Disclosure Statement. However, if any fee is due the amount of such fee may be charged to Deposit Account No. 19-4709. Applicant respectfully submits that this application is in condition for allowance. Early and favorable action is earnestly solicited.

Respectfully submitted,



Matthew W. Siegal
Registration No. 32,941
Attorney for Applicants
Stroock & Stroock & Lavan LLP
180 Maiden Lane
New York, New York 10038
(212) 806-5400

FORM PTO 1449 (modified) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE LIST OF REFERENCES CITED BY APPLICANT(S) (Use several sheets if necessary)				ATTY DOCKET NO. 000605.0002		APPLICATION NO. 10/510,355	
APPLICANT Schubert et al.				FILING DATE April 28, 2005		GROUP 1648	

U.S. PATENT DOCUMENTS							
EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE	
	6,927,217	10/01/2001	Adams	514	18	1/25/2000	
	2004/0106539	06/03/2004	Schubert	514	2	10/11/2001	

FOREIGN PATENT DOCUMENTS							
DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO/ OR ABSTRACT		
WO 99/22729	10/29/1998	WO	A61K4 5/00		NO		
DE 101 49 398	10/03/2001	DE	A61K4 5/00		Abstract		
WO 96/13266	10/27/2095	WO	A61K3 1/535		NO		
WO 02/30455	04/18/2002	WO	A61K3 8/58		Abstract		

OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)	
	Adams, J; Behnke, M; Chen, S; Cruickshank, AA; Dick, RL; Grenier, L; Klunder, JM; Ma, Y. T; Plamondon, L; Stein, RL (1998). Potent and selective inhibition of the proteasome: dipeptidyl boronic acids. <i>Bioorg. Med. Chem. Lett.</i> 8:333-338.
	Adams, J; Palombella, VJ; Sausville, EA; Johnson, J; Destree, A; Lazarus, DD; Maas, J; Pien, CS; Prakash, S; Elliott, PJ (1999). Proteasome inhibitors: a novel class of potent and effective antitumor agents. <i>Cancer Res.</i> 59:2615-2622.
	Adams, J; Palombella, VJ; Elliot, PJ (2000). Proteasome inhibition: a new strategy in cancer treatment. <i>Investigational New Drugs</i> 18:109-121.
	Adams, J; Stein, R (1996). Novel inhibitors of the proteasome and their therapeutic use in inflammation. <i>Annu. Rep. Med. Chem.</i> 31:279-288.
	Agnello, V, Abel, G, Elfahal, M, Knight, GB, Zhang, QX; (1999). Hepatitis C virus and other flaviviridae viruses enter cells via low density lipoprotein receptor. <i>Proc Natl Acad Sci USA.</i> 96:12766-71.

	Agnello, V; (2000). Mixed cryoglobulinemia and other extrahepatic manifestations of hepatitis C virus infections. In: Liang, TJ, Hoonagle JH, eds. <i>Hepatitis C</i> . San Diego: Academic Press: 295-314.
	Baldwin, AS (1996). The NF-kappa B and I kappa B proteins: new discoveries and insights. <i>Annu. Rev. Immunol.</i> 14 :649-683.
	Barton, DJ, Flanagan JB; (1993). Coupled translation and replication of poliovirus RNA <i>in vitro</i> : synthesis of functional 3D polymerase and infectious virus. <i>J. Virol.</i> 67 : 822-831.
	Behrens, SE, Grassmann, CW, Thiel, HJ, Meyers, G, Tautz, N; (1998). Characterization of an autonomous subgenomic RNA-replicon of a pestivirus. <i>J. Virol.</i> 72 : 2364-2372.
	Bukh, J, Miller RH, Purcell, RH; (1995). Genetic heterogeneity of hepatitis C virus: quasispecies and genotypes. <i>Sem. Liver Dis.</i> 15 : 41-63.
	Burke, DS, Monath, TP; (2001). Flaviviruses. In: <i>Virology</i> , fourth edition edited by B.N. Fields, Lippincott-Raven Philadelphia, New York: 1043-1125.
	Ciechanover, A (1998). The ubiquitin-proteasome pathway: on protein death and cell live. <i>EMBO J.</i> 17 :7151-7160.
	Ciechanover, A, Orian, A, Schwartz, AL; (2000). The ubiquitin-mediated proteolytic pathway: mode of action and clinical implications. <i>J. Cell Biochem. Suppl.</i> 34 : 40-51.
	Coux, O; Tanaka, K; Goldberg, AL (1996). Structure and functions of the 20S and 26S proteasomes. <i>Annu. Rev. Biochem.</i> 65 : 801-847.
	Dubuisson, J, Hsu, HH, Cheung, RC, Greenberg, HB, Russell, DG, Rice, CM; (1994). Formation and intracellular localization of hepatitis C virus envelope glycoprotein complexes expressed by recombinant vaccinia and Sindbis virus. <i>J. Virol.</i> 68 : 6147-6160.
	Elliott, PJ, Ross JS; (2001). The proteasome: a new target for novel drug therapies. <i>Am J Clin Pathol.</i> 116 :637-46.
	Elliott, PJ; Pien, CS; McCormack, TA; Capman, ID; Adams, J (1999). Proteasome inhibition: a novel mechanism to combat asthma. <i>J. Allergy Clin. Immunol.</i> 104 : 294-300.
	Fenteany, G; Standaert, RF; Lane, WS; Choi, S; Corey, EJ; Schreiber, SL (1995). Inhibition of proteasome activities and subunit-specific amino-terminal threonine modification by lactacystein. <i>Science</i> 268 : 726-731.
	Frankel, A; Man, S; Elliott, P; Adams, J; Kerbel, RS (2000). Lack of multicellular drug resistance observed in human ovarian and prostate carcinoma treated with the proteasome inhibitor PS-341. <i>Clinical Cancer Res.</i> 6 :3719-3728.
	Fuerst, TR, Niles, EG, Studier, FW, Moss B; (1986). Eukaryotic transient-expression system based on recombinant vaccinia virus that synthesizes bacteriophage T7 RNA polymerase. <i>Proc. Natl. Acad. Sci. USA</i> 83 : 8122-8126.
	Grassmann, CW, Isken, O, Behrens SE; (1999). Assignment of the multifunctional NS3 protein of bovine viral diarrhea virus during RNA replication: an <i>in vivo</i> and <i>in vitro</i> study. <i>J. Virol.</i> 73 : 9196-9205.
	Grassmann, CW, Isken, O, Tautz, N, Behrens SE; (2001). Genetic analysis of the pestivirus nonstructural coding region: defects in the NS5A unit can be complemented <i>in trans</i> . <i>J. Virol.</i> 75 : 7791-7802.
	Hanada, M; Sugawara, K; Kaneta, K; Toda, S; Nishiyama, Y; Tomita, K; Yamamoto, H; Konishi, M; Oki, T (1992). Epoxomicin, a new antitumor agent of microbial origin. <i>J. Antibiot. (Tokyo)</i> 45 :1746-1752.
	Harty, RN; Brown, ME; Wang, G; Huibregtse, J; Hayes, FP; (2000). A PPxY motif within the VP40 protein of Ebola virus interacts physically and functionally with a ubiquitin ligase: implications for filovirus budding. <i>Proc. Natl. Acad. Sci. USA</i> 97 : 13871-13876.
	Hershko, A; Ciechanover, A; (1998). The ubiquitin system. <i>Annu. Rev. Biochem.</i> 67 : 425-479.
	Higashitsuji, H; Itoh, K; Nagao, T; Dawson, S; Nonoguchi, K; Kido, T; Mayer, RJ; Arai, S; Fujita, J; (2000). Reduced stability of retinoblastoma protein by gankyrin, an oncogenic ankyrin- repeat protein overexpressed in hepatomas. <i>Nat Med.</i> 6 :96-99.
	Koeck J, Nassal M, MacNelly S, Baumert TF, Blum HE, von Weizsaecker F; (2001). Efficient infection of primary <i>Tupaia</i> hepatocytes with purified human and woolly monkey hepatitis B virus. <i>J. Virol.</i> 75 :5084-5089.
	Krueger, M; Beger, C; Welch, PJ; Barber, JR; Manns, MP; Wong-Staal, F; (2001). Involvement of Proteasome α -Subunit PSMA7 in Hepatitis C Virus Internal Ribosome Entry Site-Mediated Translation;

	<i>Mol. Cell. Biol.</i> Vol. 21 No. 24, p 8357-8364.
	Lohmann, V, Koerner, F, Koch, JO, Herian, U, Theilmann, L., Bartenschlager R; (1999). <i>Science</i> 285 :110-113.
	Lightcap, ES; McCormack, TA; Pien, CS; Chau, V; Adams, J; Elliott, PJ (2000). Proteasome inhibition measurements: clinical application. <i>Clin. Chem.</i> 46 :673-683.
	Lindenbach, BD, Rice, CM; (2001). Flaviviridae: the viruses and their replication. In: <i>Virology</i> , fourth edition edited by B.N. Fields, Lippincott-Raven Philadelphia, New York: 991-1042.
	Major, ME, Rehmann, B, Feinstone, SM; (2001). Hepatitis C viruses. In: <i>Virology</i> , fourth edition edited by B.N. Fields, Lippincott-Raven, Philadelphia, New York: 1127-1161.
	Meng, L; Kwok, BH; Sin, N; Crews, CM (1999a). Eponemycin exerts its antitumor effect through the inhibition of proteasome function. <i>Cancer Res.</i> 59 :2798-2801.
	Meng, L; Mohan, R; Kwok, BH; Elofsson, M; Sin, N; Crews, CM (1999b). Epoxomicin, a potent and selective proteasome inhibitor, exhibits <i>in vivo</i> antiinflammatory activity. <i>Proc. Natl. Acad. Sci. USA.</i> 96 (18): 10403-10408.
	Merola, M, Brazzoli, M, Cochiarella, F, Heile, JM, Helenius, A, Weiner, AJ, Houghton, M, Abrignani, S; (2001). Folding of Hepatitis C Virus E1 glycoprotein in a cell-free system. <i>J. Virol.</i> 75 :11205-11217.
	Meyers, G, Tautz, N, Becher, P, Thiel, H-J, Kuemmerer BM; (1996). Recovery of cytopathogenic and noncytopathogenic bovine viral diarrhea viruses from cDNA constructs. <i>J. Virol.</i> 70 : 8606-8613.
	Moormann, RJM, van Gennip, HGP, Miedema, GKL, Hulst, MM, van Rijn PA; (1996). Infectious RNA transcribed from an engineered full-length cDNA template of the genome of a pestivirus. <i>J. Virol.</i> 70 : 763-770.
	Moradpour, D; Grabscheid, B; Kammer, AR; Schmidtke, G; Groettrup, M; Blum, HE; Cerny, A (2001). Expression of hepatitis C virus proteins does not interfere with major histocompatibility complex class I processing and presentation in vitro. <i>Hepatology</i> 33 :1282-1287.
	Palombella, VJ; Conner, EM; Fuseler, JW; Destree, A; Davis, JM; Laroux, FS; Wolf, RE; Huang, J; Brand, S; Elliott, PJ; Lazarus, D; McCormack, T; Parent, L; Stein, R; Adams, J; Grisham, MB; (1998). Role of the proteasome and NF-kappaB in streptococcal cell wall-induced polyarthritis. <i>Proc. Natl. Acad. Sci. USA</i> 95 :15671-15676.
	Palombella, VJ; Rando, OJ; Goldberg, AL; Maniatis, T; (1994). The ubiquitin-proteasome pathway is required for processing the NF-kappa B1 precursor protein and the activation of NF kappa B. <i>Cell</i> 78 :773-785.
	Pamer, E; Cresswell, P; (1998). Mechanisms of MHC class I-restricted antigen processing. <i>Annu. Rev. Immunol.</i> 16 :323-358.
	Patnaik, A, Chau, V, Wills, JW; (2000). Ubiquitin is part of the retrovirus budding machinery. <i>Proc. Natl. Acad. Sci. USA</i> 97 :13069-13074.
	Pietschmann, T, Lohmann, V, Kaul, A, Krieger, N, Rinck, G, Rutter, G, Strand, D, Bartenschlager, R; (2002) Persistent and transient replication of full-length hepatitis C virus genomes in cell culture. <i>J. Virol.</i> 76 :4008-21.
	Phillips, JB; Williams, AJ; Adams, J; Elliott, PJ; Tortella, FC (2000). Proteasome inhibitor PS-519 reduces infarction and attenuates leukocyte infiltration in a rat model of focal cerebral ischemia. <i>Stroke</i> 31 :1686-1693.
	Rehmann, B; Ferrari, C; Pasquinelli, C; Chisari, FV (1996). The hepatitis B virus persists for decades after patients' recovery from acute viral hepatitis despite active maintenance of a cytotoxic T-lymphocyte response. <i>Nat Med.</i> 2 :1104-1108.
	Rock, KL; Gramm, C; Rothstein, L; Clark, K; Stein, R; Dick, L; Hwang, D; Goldberg, AL (1994). Inhibitors of the proteasome block the degradation of most cell proteins and the generation of peptides presented on MHC class I molecules. <i>Cell</i> 78 :761-771.
	Rock, KL; Goldberg, AL (1999). Degradation of cell proteins and the generation of MHC class I-presented peptides. <i>Annu. Rev. Immunol.</i> 17 :739-779.
	Ruemenapf, T., Unger, G, Strauss, JH, and Thiel, HJ; (1993). Processing of the envelope glycoproteins of pestiviruses. <i>J. Virol.</i> 67 : 3288-3294.
	Schubert, U; Anton, LC; Gibbs, J; Norbury, CC; Yewdell, JW; Bennink, JR (2000b). Rapid degradation of a large fraction of newly synthesized proteins by proteasomes. <i>Nature</i> 404 :770-774.
	Schubert, U; Ott, DE; Chertova, EN; Welker, R; Tessmer, U; Princiotta, MF; Bennink, JR; Krausslich, H-

	G; Yewdell, JW (2000a). Proteasome inhibition interferes with gag polyprotein processing, release, and maturation of HIV-1 and HIV-2. <i>Proc. Natl. Acad. Sci. USA</i> 97:13057-13062.
	Schwartz, AL; Ciechanover, A (1999). The ubiquitin-proteasome pathway and pathogenesis of human diseases. <i>Annu. Rev. Med.</i> 50:57-74.
	Strack, B; Calistri, A; Accola, MA; Palu, G; Goettlinger, HG (2000). A role for ubiquitin ligase recruitment in retrovirus release. <i>Proc. Natl. Acad. Sci. USA</i> 97:13063-13068.
	Suzuki, R; Tamura, K; Li, J; Ishii, K; Matsuura, Y; Miyamura, T; Suzuki, T (2001). Ubiquitin mediated degradation of hepatitis C virus core protein is regulated by processing at its carboxyl terminus. <i>Virology</i> 280:301-309.
	Teicher, BA; Ara, G; Herbst, R; Palombella, VJ; Adams, J (1999). The proteasome inhibitor PS-341 in cancer therapy. <i>Clin. Cancer Res.</i> 5:2638-2645.
	Thiel, HJ, Plagemann, PGW, Moennig, V; (1996). Pestiviruses. In B.N. Fields, D.M.Knipe, and P.M. Howley (ed.), <i>Fields virology</i> . Raven Press, Philadelphia. Pa.: 1059-1074.
	Trautwein, C; Manns, M (2001). Antivirale Therapie der chronischen Virushepatitis. <i>Internist</i> 42:913-923.
	Yagi, T; Hardin, JA; Valenzuela, YM; Miyoshi, H; Gores, GJ; Nyberg, SL (2001). Caspase inhibition reduces apoptotic death of cryopreserved porcine hepatocytes. <i>Hepatology</i> 33:1432-40.
	Yu, H, Grassmann, CW, Behrens SE; (1999). Sequence and structural elements at the 3' terminus of bovine viral diarrhea virus genomic RNA: functional role during RNA replication. <i>J. Virol.</i> 73: 3638-3648.
	Yu, H, Isken, O, Grassmann, CW, Behrens SE; (2000). A stem-loop motif formed by the immediate 5'-terminus of the bovine viral diarrhea virus genome modulates translation as well as replication of the viral RNA. <i>J. Virol.</i> 74: 5825-5835.
	Zhao, X, Tang Z, Klumpp B, Wolff-Vorbeck, G, Barth H, Levy S, von Weizsaecker, F, Blum HE, Baumert TF; (2002). Primary hepatocytes of <i>Tupaia belangeri</i> as a potential model for hepatitis C virus infection <i>J. Clin. Invest.</i> 109: 221-232.
EXAMINER	DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.